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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
GALITSKY, NIKOLAI M

ART UNIT	PAPER NUMBER
1631	8

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/685,961	RAMBAUD, PATRICK	
	Examiner	Art Unit	
	Nikolai M Galitsky	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Peri d for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31,35 and 36* is/are pending in the application.

4a) Of the above claim(s) *10-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,20-31,35 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-31,35 and 36* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) [redacted] No(s) *Page 1* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION.

As per restriction requirement set forth in the previous Office action dated 02/26/2002, applicant has elected, without traverse, the Group I, claims 1-31, 35 and 36, specie A. Claims 32-34 has been canceled. Claims 10-19 are withdrawn from examination at this time as being directed to non-elected subject matter. Claims herein under examination are claims 1-9, 20-31, 35 and 36.

Priority

Acknowledgment is made of applicants' claim the right to priority under 35 U.S.C. § 119(a) and 37 CFR § 1.55 (a) based on France application serial No. 0000804, filed January 21, 2000.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9, 20-31, 35 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Te rejection is applied for the following reasons:

A. The expression "immunity information" in claims, such as 1, 6-7, 23, 28, 35 and 36, directly or indirectly via dependence, renders the claims indefinite. The expression " immunity information " is not defined in the claims, the specification does not provide a clear definition, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. Therefore, said term is vague and indefinite as to whether actual chemical or physical information is included.

B. Claim 1 (lines 10 and 13): the "information characteristic" implies that the characteristic is chosen by some kind of criteria and implied criterion is critical in applying it to "gathering and processing information", and therefore it is unclear. Applicant can resolve this issue by particularly pointing out what characteristic is chosen.

C. The term "status-characterizing" in claims, such as 2-9, 24, 25, 29 and 30 are a relative term, which renders the claim indefinite. The term "status-characterizing" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention.

D. Claims 8 and 30: the "optimal proportions" implies that the proportions are chosen by some kind of criteria and implied criterion is critical in applying it to the "different immunocompetent cells in view of their deferred use", and therefore it is unclear. Applicant can resolve this issue by particularly pointing out what optimal proportion is optimal.

E. Claims 9 and 31: the "optimal ratio" implies that the ratio is chosen by some kind of criteria and implied criterion is critical in applying it to the "lymphocytes T4 and T8 in view of their deferred use", and therefore it is unclear. Applicant can resolve this issue by particularly pointing out what optimal ratio is optimal.

F. The term "elements" in claims 5 and 27, directly or indirectly via dependence, renders the claims indefinite. The term "elements" is not defined in the claims, the specification does not provide a clear definition, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. Therefore, said term is vague and indefinite as to whether actual chemical or physical information is getting from a capillary study of the human or animal subject's hair system.

G. The term "expert system" in claims 7 and 28 directly or indirectly via dependence, renders the claims indefinite. The term "expert system" is not defined in the claims, the specification does not provide a clear definition, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. Therefore, said term is vague and indefinite as to whether actual chemical or physical information is used for an interpretation of the status with respect to a particular gene.

H. The term "initial step" in claims 20 (line 3) and term "annihilation" in the claim 21, directly or indirectly via dependence, renders the claims indefinite. The terms "initial step" and "annihilation" are not defined in the claims, the specification does not provide a clear definition, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. Therefore, said terms are vague and indefinite as to what the initial step means for cryogenizing the batch and whether actual chemical or physical methods are used in step for checking the "annihilation" of the antibodies within the batch.

I. The term "sequence" in claim 22 (line 2), directly or indirectly via dependence, renders the claims indefinite. The term "sequence" is not defined in the claims, the specification does not provide a clear definition, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. Therefore, said term is vague and indefinite as to what kind of sequence for conditioning a batch is applied in the steps of the selecting purified lymphocytes or monocytes?

J. The term "sensible crystallization image" in claim 26 (lines 2 and 3), directly or indirectly via dependence, renders the claims indefinite. The term " sensible crystallization image" is not defined in the claims, the specification does not provide a clear definition, and one

of ordinary skill in the art would not be reasonably appraised of the scope of the invention. Therefore, said term is vague and indefinite as to whether actual chemical, or physical, etc., information is included in the crystallization images of blood, which was previously collected on the human or animal objects for getting bio-electronic information.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless --

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 23, 35 and 36 are rejected under 35 U.S.C. § 102(a) as being clearly anticipated by Lefesvre, (WO 99/53030, 21 October 1999).

In the absence of English language translation of Lefesvre, WO 99/53030, 21 October 1999, the Derwent database abstract was used also (Lefesvre, Database Derwent-Acc-No: 1999-620413, 01 November 1999).

Claims 1 and 23 are drawn to a method and system for managing batches of immunocompetent cells collected from human or animal subjects for deferred use. The reference describes (See Lefesvre, WO 99/53030, 21 October 1999), in abstract, lines 4-10, a method for managing immunocompetent cell batches belonging to human subject from whom said sets have removed for future use on said subject or relatives. Each immunocompetent cell batch associated with a subject is packaged and stored in a cryogenic site among a plurality of cryogenic sites, then transferred on request to a cell treatment center. Said method provides individual preservation of immunocompetent elements and the possibility, if it is so desired, of culturing them with growth thereof. It aims at protecting the immunity and generic capital from

being altered during the individual's lifetime. The invention is particularly useful for reinforcing immune activity and gene therapy.

Claims 35 and 36 are rejected under 35 U.S.C. § 102(a) as being clearly anticipated by Lefesvre, (Database Derwent-Acc-No: 1999-620413, 01 November 1999)

Claims 35 and 36 are drawn to a method and system for determining parameters of a protocol for deferred use of immunocompetent cells from human or animal subject's personal library. The reference describes (See Lefesvre, Database Derwent-Acc-No: 1999-620413, 01 November 1999, in an abstract, lines 1-24), the process [protocol] for managing batches of immunocompetent cells, taken from a human subject and intended for reuse at some later time, comprises the following:

(i) packaging and storing batches of cells, taken at successive times, it one or more storage centers;

(ii) preparation and updating of a personal library of (A) from the samples taken, this library containing all the information on immunity contained in the samples cells; and

(iii) when required, treatment of at least some of this information, locating one or more batches and transfer of them from storage to a cellular treatment center for reuse.

There is also description of a system for managing batches.

The stored cells are particularly used for:

(i) for increasing, or restoring, cellular immunity (e.g. for prevention or treatment of uncontrolled acute infection, persistence of chronic infection, malignancy or disease of the immune system itself);

(ii) for producing transfer factors;

(iii) for gene therapy;

(iv) for performing genetic analysis (e.g. to identify mutations); and

(v) to detect signs of infection that were not recognized when the sample was taken.

The method makes it possible to store cells, in readily accessible and identifiable form, for very long periods, e.g. for decades. Storage in batches eliminates the need to thaw a large quantity of cells (greater than needed for a particular application)."

Claims Rejected Under 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Although the inventions are not identically disclosed or described as set forth 35 U.S.C. 102, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a designer having ordinary skill in the art to which said subject matter pertains, the invention is not patentable.

Claims 2-9, 20-22 and 24-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lefesvre, (WO 99/53030, 21 October 1999) in view of Shiota et al. (Special Capabilities of Micro-Multiplane Transesophageal Echocardiography for Studying Congenital Heart Disease Surgery in Neonates, Infants and Children. Journal of the American College of Cardiology,February 1998, Volume 31, Issue 21001, Supplement 1, pages 247A-248A), or in view of Egger et al. (Changes in the polymorphonuclear leukocyte function of blood samples induced by storage time, temperature and agitation. Journal of Immunological Methods. 07 August 1997, Volume 206, Issue 1-2, pages 61-71.), or in view of Connelly et al. (The clinical

workstation as a means of improving laboratory use. Clinica Chimica Acta. 15 April 1996, Volume 248, Issue 1, pages 51-64), or in view of Lakew et al. (Combined immunomagnetic cell sorting and ELISPOT assay for the phenotypic characterization of specific antibody-forming cells. Journal of Immunological Methods. 25 April 1995, Volume 203, Issue 2, pages 193-198), or in view of Nicolini C. (Supramolecular architecture and molecular bioelectronics. Thin Solid Films. 15 September 1996, Volume 284-285, pages 1-5), or in view of Stoylova et al. (Structural determination of lipid-bound human blood coagulation factor IX. Biochimica et Biophysica Acta (BBA)/Protein Structure and Molecular Enzymology. 02 April 1998, Volume 1383, Issue 2, pages 175-178), or in view Pio et al. (Granule associated DNase in T4 and T8 lymphocytes from patients with autoimmune diseases. Biochimica et Biophysica Acta (BBA)/Molecular Basis of Disease. 27 February 1998, Volume 1406, Issue 1, pages 51-61), or in view of Plantikow-Voßgätter et al.(Application of an ETV-ICP system for the determination of elements in human hair. Spectrochimica Acta Part B: Atomic Spectroscopy. 30 January 1996, Volume 51, Issue 2, pages 261-270).

The primary reference is used as discussed above. The reference does not specifically teach all particular methods of characterizing immunocompetent cells, methods of collecting and processing information as instantly claimed. If there are any differences between Applicant's claimed methods and that of the prior art, the differences would be appear minor in nature. It would be conventional and within the skill of the art to define immunocompetent cells of interest and methods of their characterization.

For example:

(1) The claims 2 –9, 24, and 28-30 recite limitation of the status-characterizing information of blood. Shiota et al. (See page 247A, lines 5-6) are detailed information about anatomy [status] and blood flows characterizing their pre- or postoperative conditions were obtained using... rotational imaging.

(2) The claims 2 and 24 recite limitation of processing a blood samples. Egger et al., (see page 61, lines 1-2 and 13-15), are investigated changes in polymorphonuclear leukocyte (PMN) functions of blood samples caused by such typical elements of laboratory handling as storage time, temperature and agitation. In order to obtain reliable results from PMN functional tests, whole-blood assays and processing of blood samples within 20 min after blood withdrawal are recommended.

(3) The claims 6,7, 24 and 28 recite limitation of an expert system. Connelly et al. , describes clinicians' workstation (CWS) is meant to provide doctors and nurses ready access to laboratory results in a form that makes the data easy to review and use. In addition, the workstation provides immediate feedback regarding blood orders, to encourage appropriate clinical practice. Feedback is based on the medical staff's clinical guidelines that have been incorporated into an embedded expert system. CWS also helps blood bank physicians to monitor, review and control requests for special needs such as irradiated products. Challenges to system acceptance await those trying to bring functional decision support to the clinical environment. Among these are barriers to understanding and cooperation posed by departmental boundaries and interacting professional cultures as well as the politics of hospital-based information systems.

(4) The claims 20-22 recite limitation of checking the annihilation of the antibodies within the batch. Lakew et al., describes (see abstract, lines 3-4) a combination of immunomagetic cell

sorting [selecting] and ELISPOT techniques has been evaluated [checking] to permit enrichment and characterization of antibody-secreting cells (ASC). Cell suspensions containing putative ASC were first incubated with magnetic microbeads coated with antibodies specific for a given cell surface marker. After separation of bead-cell clusters and free cells, the resulting cell populations were examined for the presence of ASC by an ELISPOT assay.

(5) The Claims 3 and 25 recite limitation to the system for getting bio-electronic information of blood previously collected on the human or animal subject. Nicolinni C. on the page 4, column 2, lines 30-35, introduces molecular bioelectronics as a new field at the interface of molecular biology and microlectronics, emerging from supramolecular architectures of different biological materials. Thus, it would have been obvious to some one of ordinary skill in the art at the time of the instant invention to use a method for managing immunocompetent cell batches motivated by Lefesvre, (WO 99/53030, 21 October 1999) to additionally practice molecular bioelectronics for getting bioelectronic information of the blood on the human or animal subject, thus resulting in the practice of the instant invention.

(6) The Clams 4 and 26 recite limitation to the system for getting information by processing sensible crystallization images of blood. Stoylova et al., describes on page 175, in abstract human coagulation factor IX (FIX) is a serine protease, which binds to a negatively charged phospholipid surface in the presence of Ca ions (Ca2+). FIX two-dimensional (2-D) crystals were obtained by the lipid layer crystallization technique under near physiological conditions. The 2-D projection map of the protein was calculated to a resolution of 3 nm using electron crystallographic analysis. And also on page 175, column 2, lines 4-6, Stoylova et al., describes electron crystallogphy as a powerful method to determine the structural organization of

biological macromolecules and on the page 176, column 2 lines 6-7 the Pc-based crystallographic image processing software package. Stoylova et al., noted on page 177, column2, lines 45-47 the approaches presented will also open a vast field in study of the macromolecular organization of a blood coagulation complexes.

(7) The claims 8, 9, 30 and 31 recite limitation of an optimal ratio between lymphocytes T4 and T8. Pio at al., describes (see page 51, lines1-12) a DNase activity associated with secretion granules was detected in T4 and T8 lymphocytes from patients with autoimmune diseases. This activity was much higher in primary biliary cirrhosis (PBC) than in Graves' disease (GD) and multiple sclerosis (MS) or in healthy subjects. This granule associated DNase activity was Ca2+-dependent, inhibited by Zn2+, and higher at low pH; its molecular weight corresponded to 66kDa; it was more active with double-strand than single-strand DNA. Judging from its properties this enzyme differed from the three types of endonucleases described as involved in DNA fragmentation (DNase I, DNase II and NUC18). Flow cytometry analysis of T lymphocytes showed that DNase activity associated with CD4+ lymphocyte granules correlated with the ratio CD4+CD45RO+/CD4+CD45RA+ (memory and cytotoxic cells/naive cells, inducers of suppression). In contrast, T8 lymphocyte DNase activity correlated with the proportion of CD4+ lymphocytes with CD4+CD45RA- phenotype (helpers and inducers of cytotoxicity). The possible role of this DNase activity in the mechanisms of lysis or apoptosis mediated by CTL is discussed. We suggest that this DNase activity could be implicated in some of the alterations of the autoimmune response depending on cytotoxic T lymphocytes or T cell inducers of apoptosis.

(8) The claim 27 recites limitation of elements of the human or animal subject's hair system. Plantikow-Voßgätter et al. describes (on the page 261,lines 1-4) the determination [study] of an element contents in hair samples without sample digestion it is necessary to analyze large sample volumes in order to minimize problems of inhomogeneity of biological sample materials. Therefore an electrothermal vaporization system (ETV) is used for solid sample introduction into an inductively coupled plasma (ICP) for the determination of matrix and trace elements in hair.

Thus, the selection of appropriate methods of characterizing immunocompetent cells, and/or methods of collecting and processing information as instantly claimed are conventional and within the skill in the art to which this invention pertains. It would have been obvious to some one of ordinary skill in the art at the time of the instant invention to use a method for managing immunocompetent cell batches motivated by Lefesvre, (WO 99/53030, 21 October 1999) to additionally practice methods of characterizing immunocompetent cells, and/or methods of collecting and processing information, thus resulting in the practice of the instant invention.

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nikolai M Galitsky, Ph.D., whose telephone number is (703) 308-2422. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst, Bill Phillips, whose telephone number is (703) 305-3482 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

June 13, 2002

MICHAEL BORIN, PH.D
PRIMARY EXAMINER